Amend claim 61 to read as follows:

61. (Twice amended) An implantable anti-infective medical device selected from the group consisting of catheters, prostheses, shunts, stents, and leadwires, comprising a solid polymeric matrix selected from the group consisting of thermoplastic polymers and thermosetting polymers, containing within the matrix solid particles of an oxidant-producing component comprising a reducing agent and an oxidizing agent that, when wetted, causes the formation of an oxidant and sustained release of the thus-formed oxidant into and about the polymeric matrix so that the matrix serves as an anti-infective reservoir.

Add claim 112 to read as follows:

112. The anti-infective medical device of claim 61 selected from the group consisting of catheters and prostheses.

REMARKS

Applicants' attorney thanks Examiner Choi for the courtesy of an informal copy of the Advisory Action mailed June 13, 2003, as this Advisory Action has not yet been received by mail.

Entry of this amendment is respectfully requested. No new matter is added by the amendment, as the amended claim 61 and added claim 112 are fully supported by the application as filed. A version of the amended claim 61 showing the changes made from the application as it existed prior to this amendment is attached.

This amendment to claim 61 is identical to the amendment mailed April 18, 2003, which was not entered. In the Advisory Action, the Examiner indicated with respect to the amendment that:
(1) the amendment appeared to raise an issue of new matter with respect to the limitation to "shunts, stents, and leadwires", where the Examiner could not locate support for that limitation in the application. Applicants submit that limitation of the claims to implantable medical devices that are "catheters, prostheses, shunts, stents, and leadwires" (claim 61) is not new matter in view of the disclosure at page 1, lines 15-17, of the application, which states "Implanted medical devices (*e.g.*, venous and arterial catheters, neurological prostheses, shunts and stents, joint implant prostheses, urinary "Foley" catheters, peritoneal catheters, lead wires to pacemakers, etc.), ... ". Thus catheters, prostheses, shunts, stents, and leadwires are described in the application as exemplary of implantable medical devices. Applicants also note that the discussion in the paragraph bridging pages 30 and 31, and especially at page 31, lines 9-14, refers to coverings over catheter leadwires as well as to catheters and other forms. Thus, the limitation introduced into claim 61 does not constitute new matter;
(2) the amendment appeared to raise a 35 USC 112, ¶2 issue with respect to a statement in the "Remarks" that "the present invention permits the simultaneous incorporation of a reducing agent and an oxidizing agent by the mixing of solid particles into the polymer (or polymer precursors)." The Examiner indicates that "the claims do not require the reducing agent and oxidizing agent be added as solid particles only that the final product contain solid particles". Applicants agree that the claims do not require the mixing of solid particles into the polymer but only that the final product contain solid particles; however, this is not seen to raise an issue under 35 USC 112, ¶2, because mixing of solid

particles into the polymer or polymer precursor is a technique disclosed in the application for producing the final product containing solid particles (*see*, for example, the paragraph bridging pages 30 and 31 of the application).

Claims 61, 62, 64 - 76, and 99 - 112 are in this application, claims 77 - 98 having been canceled, claim 61 having been amended, and claim 112 having been added by this submission. Claims 61, 62, 64 - 69, 73 - 76 [the Office Action refers to 73 - 75, but Applicants note that claim 76 reads on the elected invention, where the polymeric matrix comprises a hydrophobic polymer, *see* the Response of February 19, 2002, page 8, where "a hydrophobic polymer that is a silicone polymer" was elected], 92, 93, 95, 96, 99 - 104, and 109-111 were under examination, and were rejected under 35 USC 103(a). The rejection is respectfully traversed in view of the amendment.

The 35 USC 103(a) rejection

Claims 61, 62, 64 - 69, 73 - 75, 92, 93, 95, 96, 99 - 104, and 109-111 were rejected under 35 USC 103(a) as being unpatentable over Montgomery et al., US Patent No. 4,576,817, in view of Kams, US Patent No. 1,867,222. This rejection, as applied to the amended and added claims, is respectfully traversed.

The invention

The invention of the present application, as defined by the broadest claim 61, is an implantable anti-infective medical device selected from the group consisting of catheters, prostheses, shunts, stents, and leadwires, comprising a polymeric matrix selected from the group consisting of thermoplastic polymers and thermosetting polymers, containing within the matrix solid particles of an oxidant-producing component comprising a reducing agent and an oxidizing agent that, when wetted, causes the formation of an oxidant and sustained release of the thus-formed oxidant into and about the polymeric matrix so that the matrix serves as an anti-infective reservoir.

Elected dependent claims specify the oxidant, the oxidant-producing component, the presence of a proton donor and its nature, the nature of the device, and the like.

The invention is particularly advantageous as it provides implantable medical devices having anti-infective activity which are energizable generally simply by implantation and provide sustained release of an anti-infective oxidant so that the device serves as an anti-infective reservoir, helping to prevent the infections commonly associated with implantable medical devices.

Montgomery et al.

Montgomery et al. discloses enzymatic absorbent materials such as bandages and pads for body contact applications containing a serum-activated oxidoreductase enzyme (such as glucose oxidase). The enzymatic material may also contain a peroxidase enzyme and an oxidizable substrate (such as a substrate specific to the oxidoreductase enzyme and a thiocyanate, chloride, or iodide salt). The enzymatic absorbent materials may be prepared from standard absorbent precursors (such as woven fibers, porous foam pads, absorbent membranes, and solvent-based porous elastomers, gauze bandaging, etc.) or the enzyme may be incorporated into absorbent fibers and these fibers converted into bandages or pads.

Montgomery et al. does not disclose the use of an oxidizing agent such as iodate, or the use of iodate as an iodine source.

Further, the Examiner notes that Montgomery states that a contraceptive flexible foam pad can be obtained "by incorporating spermicidal composition in the invention". The clear implication from

this is that the formulation of Montgomery et al. as described (i.e. containing the oxidoreductase enzyme and optionally the peroxidase enzyme and oxidizable substrate) is not in itself spermicidal.

Karns

Karns discloses a surgical dressing that will release iodine on application to a moist wound or upon being moistened by water. The dressing comprises a web of surgical gauze or the like impregnated in part of its extent with iodine-containing material (such as an iodide or an iodate or periodate) and impregnated in another part with an iodine-releasing material (such as an oxidizing agent and an acid if the iodine-containing material is an iodide, or a reducing agent if the iodine-containing material is an iodate or periodate). The web is impregnated partwise with the solutions of the two materials, dried, and then folded so that the areas overlie one another.

Discussion

The Examiner reasons that "One with ordinary skill in the art would have been motivated to use the teachings of Karns in Montgomery because the use of an iodine-releasing material and an oxidizing material such as iodate would deliver the benefits of iodine (as an excellent antiseptic agent) while avoiding the drawbacks (loss of power). Further, one with ordinary skill would have known that such a composition would be suitable for internal body contact (as taught by Montgomery)." Applicants respectfully disagree.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one or ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), cited in MPEP 2142.

First, Montgomery et al. does not teach or suggest an implantable anti-infective medical device, comprising a solid polymeric matrix selected from the group consisting of thermoplastic polymers and thermosetting polymers, containing within the matrix solid particles of an oxidant-producing component comprising a reducing agent and an oxidizing agent that, when wetted, causes the formation of an oxidant and sustained release of the thus-formed oxidant into and about the polymeric matrix so that the matrix serves as an anti-infective reservoir. Although Montgomery does disclose the apparent incorporation of an enzyme into a fiber and a foam (Examples II and III), Applicants note that in Example II, the enzyme was found in the aqueous component of an emulsion and not in the fiber-forming organic component; and in Example III, the enzyme was also found in a dispersion, in each case in solution form. Further, these examples contain only an enzyme and do not contain a reducing agent and an oxidizing agent. The other examples disclose only deposition onto spun cotton pads, and not incorporation into the polymeric matrix.

This deficiency of Montgomery et al. is not remedied by Karns, which discloses only the absorption of active ingredients onto surgical dressings (cotton gauze and the like), and does not disclose implantable devices, as discussed earlier. Moreover, the Examiner's statements not to the contrary, there is no motivation in either Montgomery et al. or in Karns to put the iodide/iodate system of Karns into the enzymatic system of Montgomery et al. because the essence of Montgomery et al., like that of the present invention, is to have a system in which the active ingredients of the system are added simultaneously and are all present in the polymeric matrix, and the iodide/iodate system of Karns cannot be used for absorption onto the cotton gauze and like materials of Montgomery et al. in this way

because dissolution of the necessary components would result in the formation of iodine in the impregnation solution and failure of the process. Both Montgomery et al. and Kams refer to the use of solutions in the preparation of their materials, whereas the present invention permits the simultaneous incorporation of a reducing agent and an oxidizing agent by the mixing of solid particles into the polymer (or polymer precursors).

With respect to claim 76 and its dependent claims, there is no disclosure or suggestion that the polymeric matrix should be a hydrophobic polymer.

Regarding rejection of the anti-infective claims, although Montgomery et al. teaches a "...suitable oxidoreductase enzyme is glucose oxidase ..." and that "...the material can also contain iodine along with the enzyme..." as stated by the Examiner, Montgomery et al. teaches iodine generating activity aimed at treating wounds in which serum, and thus glucose, is present through application of "Enzymatic absorbent materials such as bandages and pads, for body contact applications ...upon contact of the enzymatic materials with serum..." (Abstract, see also claims 1 and 20). Montgomery et al. does not teach how glucose oxidase and iodide could be incorporated into man-made nonabsorbent synthetic polymers used to fabricate implantable medical devices. On the contrary, Montgomery makes clear that their anti-infective formulations require absorbent material (claims 1 and 20), thereby teaching away from art concerned with nonabsorbent polymeric materials addressed in these claims.

In particular, whereas the present patent filing teaches art for introducing iodine-generating chemistry through the use of dry chemical formulations co-mixed into man-made synthetic polymers used in the fabrication of implantable medical devices, the art taught by Montgomery et al. teaches the use of liquid chemical formulations for incorporation into absorbent materials. Those knowledgeable in the art are aware however that it is not feasible to include moisture in the base materials of thermoplastic and condensation polymers such as polyurethanes and polysiloxanes during extrusion and molding of medical devices because water has a highly deleterious effect on the final product. It is thus known that thermoplastic polyurethanes, for example, must be thoroughly heated and dried for several hours before the raw material can be properly melted, molded and extruded into a device. The polymerization of diisocyanate monomers with diols to produce elastomeric polyurethanes used for fabrication of medical devices likewise is adversely affected by the presence of water because water will degrade isocyanate and therefore interfere with successful polymerization and fabrication of the final product.

Furthermore, the high temperatures used in extrusion and molding of polyurethanes and polysiloxanes (>150 °C), and other thermoplastic polymers common to medical devices, negates any possibility of using the art specifically taught by Montgomery et al.. This is obvious to those of ordinary skill in the art because it is known that aqueous enzyme solutions are heat labile and not tolerant to the temperatures required for extrusion and molding of many medical devices. Nor would Montgomery et al.'s enzyme formulations tolerate the high temperatures typically encountered during sterilization of medical devices which likewise would cause denaturization of their enzyme formulations rendering the devices devoid of any possibility of expressing anti-infective activities when implanted in the body.

Also, while the devices of Montgomery et al. may be "utilizable for internally body contact devices" as described by the Examiner, Applicants note that there is a widespread medically and regulatorily recognized distinction between devices for body contact (even for internal body contact such as tampons) and devices for implantation; and it is these latter devices that are claimed in claim 61 and its dependent claims. Montgomery et al. does not speak to such devices, and the absorbent pads of Kams et al. are clearly intended only for application to external wounds and the like.

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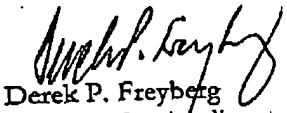
Accordingly, Montgomery et al in view of Karns do not make claims 61, 62, 64 - 69, 73 - 76, 99 - 104, and 109-111 unpatentable, and withdrawal of the rejection is requested.

Further, allowance of the nonelected claims is also requested as they are all properly dependent on allowable claim 61.

Conclusion

For the reasons given above, Applicants submit that claims 61, 62, 64 - 69, 73 - 76, 99 - 104, and 109-112 are not unpatentable over Montgomery et al in view of Karns. Entry of the amendment, and re-examination and allowance of the claims (including the non-elected claims) are respectfully requested.

Respectfully submitted,



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Amended text showing amendments made
(additions in bold, deletions struck through)

Claim 61:

61. (Twice amended) An implantable anti-infective medical device selected from the group consisting of catheters, prostheses, shunts, stents, and leadwires, comprising a solid polymeric matrix selected from the group consisting of thermoplastic polymers; and thermosetting polymers, ~~and hydrogels~~, containing within the matrix solid particles of an oxidant-producing component comprising a reducing agent and an oxidizing agent that, when wetted, causes the formation of an oxidant and sustained release of the thus-formed oxidant into and about the polymeric matrix so that the matrix serves as an anti-infective reservoir.